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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,563	02/22/2002	David M. Herrington	9151-15	2002

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EXAMINER	
SISSON, BRADLEY L	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 04/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,563	HERRINGTON ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *3-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1 and 2, in the response of 31 October 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 3-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the response of 31 October 2003.

Specification

3. The specification is objected to as documents have been improperly incorporated by reference. In particular, the specification states that some documents have been incorporated by reference in their entirety; see pages 5, 6, and 9. Such omnibus language fails to specify what specific information applicant seeks to incorporate and similarly fails to point with detailed particularity just where that specific information is to be found. As set forth in *Advanced Display Systems Inc. v. Kent State University* (Fed. Cir. 2000) 54 USPQ2d at 1679:

> Incorporation by reference provides a method for integrating material from various documents into a host document--a patent or printed publication in an anticipation determination--by citing such material in a manner that makes it clear that the material is effectively part of the host document as if it were explicitly contained therein. *See General Elec. Co. v. Brenner*, 407 F.2d 1258, 1261-62, 159 USQP 335, 337 (D.C. Cir. 1968); *In re Lund*, 376 F.2d 982, 989, 153 USPQ 625, 631 (CCPA 1967). **To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that**

> **material is found in the various documents.** *See In re Seversky*, 474 F.2d 671, 674, 177 USPQ 144, 146 (CCPA 1973) (providing that incorporation by reference requires a statement "clearly identifying the subject matter which is incorporated and where it is to be found"); *In re Saunders*, 444 F.2d 599, 602-02, 170 USPQ 213, 216-17 (CPA 1971) (reasoning that a rejection or anticipation is appropriate only if one reference "expressly incorporates a particular part" of another reference); *National Latex Prods. Co. v. Sun Rubber Co.*, 274 F.2d 224, 230, 123 USPQ 279, 283 (6th Cir. 1959) (requiring a specific reference to material in an earlier application in order to have that material considered a part of a later application); *cf. Lund*, 376 F.2d at 989, 13 USPQ at 631 (holding that **a one sentence reference to an abandoned application is not sufficient to incorporate from the abandoned application into a new application**). (Emphasis added.)

Accordingly, the cited documents are not considered to have been properly incorporated by reference and accordingly, have been considered without effect towards fulfilling the enablement, written description, and best mode requirements of 35 USC 112, first paragraph.

Response to argument

At page 9 of the response applicant asserts that the documents have been properly incorporated by reference because *inter alia*, "the references in paragraph43 refers [*sic*] to the numerous estrogen replacement therapy preparations and protocols that are commonly known in the art." The above argument ahs been fully considered and has not been found persuasive. It can be argued that any and all publications are of documents that are known in the art, as it is impossible to incorporate by reference that which has not yet been published. The aspect of whether a document is commonly known or not is not dispositive of this objection (not rejection, as asserted at page 9 of the response of 31 October 2003). It is well settled that a proper incorporation by reference requires that "the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents." Applicant has not pointed to where such indications are found

in the original disclosure. Therefore, and in the absence of convincing g evidence to the contrary, the objection to the specification has been maintained.

4. The use of the trademark TRITON X-100 has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

5. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Priority

6. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1 and 2 of this application.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed

invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

> To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Vas-Cath, 935 F.3d at 1563; see also Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

9. For convenience, claims 1 and 2 are reproduced below.

1. (Currently Amended) A method of screening a subject for increased likelihood of having a favorable response to estrogen replacement therapy with respect to cardiovascular health due to increased HDL levels, comprising:

detecting the presence of the rare form of at least one estrogen receptor alpha polymorphism in said subject, the presence of said rare form of said estrogen receptor alpha polymorphism indicating said subject is more likely to have a favorable response to estrogen replacement therapy with respect to cardiovascular health than a subject with the common form of said polymorphism;

said at least one estrogen receptor alpha polymorphism selected from the group consisting of the rare form of the IVS1-354 polymorphism, the rare form of the IVS1-401 polymorphism, the rare form of the IVS1-1415 polymorphism, and the rare form of the IVS1-1505 polymorphism.

2. (Original) A method according to claim 1, wherein said detecting step further comprises detecting whether said subject is homozygous for said rare form of said at least one estrogen receptor alpha polymorphism.

10. For purposes of examination, claims 1 and 2 have been interpreted as encompassing the screening "a subject for an increased likelihood of having a favorable response to estrogen therapy with respect to cardiovascular health due to increased HDL levels," where the "subject" is virtually any life form, including non-humans, and where the individual is biologically male of female, and is of virtually any age, including fetal, infant, preadolescent, etc.

11. A review of the disclosure fails to locate an adequate written description of where the subject is anything other than a human female

12. At paragraphs 54 to 70, applicant presents Example 1, along with the results obtained therefrom. As seen herein, only postmenopausal women with established coronary heart disease were evaluated. It is further noted that the method excluded women with triglycerides >400 mg/dl, uncontrolled diabetes or hypertension, or excessive alcohol use. At page 16 (paragraph 68) it is seen that "only non-Hispanic whites were sufficiently numerous to support an inference of interaction with confidence (P=0.023 for IVS1-401C/C versus C/T or T/T)." In view of such explicit statements by applicant, and the absence of other supporting evidence to the contrary, the specification does not provide an adequate written description of where applicant could draw "inference of interaction with confidence" with any other group of women or the same inference with respect to the same group of women, but with a different rare polymorphism. Similarly, the specification does not provide an adequate written description of where the claimed method could be practiced for any polymorphism with respect to any other subject. Such absence of an adequate written description of the claimed method does not reasonably suggest that applicant had possession of the invention at the time of filing. Accordingly, claims 1 and 2 are rejected

under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

13. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135, bridging to 1136:

> To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, *e.g.*, *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

14. It is well settled that one cannot enable that which they do not yet possess. The instant disclosure cannot rely upon cited documents as providing the enabling disclosure and the requisite starting materials. As shown above, the specification teaches that an inference of interaction has been found with respect to but a subgroup of postmenopausal non-Hispanic white women, which did not have triglycerides >400 mg/dl, uncontrolled diabetes or hypertension, or excessive alcohol use. Accordingly, the instant specification cannot now enable the generic method of screening any "subject" when such method is not reasonably in applicant's possession at the time of filing. Accordingly, claims 1 and 2 are rejected under 35 USC 112, first paragraph, as failing to comply with the enablement requirement.

While the specification does teach that other polymorphisms were evaluated, no inference of interaction with confidence could be established. The specification does not set forth reaction conditions and starting materials that are required to practice the scope of the claimed invention. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
>
> *****
>
> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing

> out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (Emphasis added)

15. For the above reasons, and in the absence of convincing evidence to the contrary, claims 1 and 2 are rejected under 35 USC 112, first paragraph, as failing to comply with the enablement requirement.

Response to argument

16. At page 10 of the response received 31 October 2003 applicant directs attention to where an inference of interaction was found to exist with respect to IVS1-401 C/C polymorphisms and yet other polymorphisms, and improved cardiovascular health, and that as a result of this showing, the full scope of the claimed method is enabled.

17. The above argument has been fully considered and has not been found persuasive as applicant has not shown which, if any of these polymorphisms as found in non-Hispanic white postmenopausal women is found in premenopausal women or any other subject, human or otherwise, and which correlates with improved cardiovascular health. While the specification

does identify other polymorphisms, it is noted with particularity that no "inference of interaction with confidence" could be established. Accordingly, applicant has not presented evidence which demonstrates that the originally field specification is fully enabling for the claimed method of screening where any rare estrogen receptor alpha polymorphism whose presence in any subject at any stage of life, and having any other preexisting condition is indicative that the subject will have a favorable response to hormone replacement therapy with respect to HDL levels. Accordingly, and in the absence of convincing evidence to the contrary, the rejection is maintained.

18. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

19. Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

20. Claims 1 and 2 are indefinite with respect to what constitutes "the rare form of the 1V51-354 polymorphism, the rare form of the 1VS1-401 polymorphism, the rare form of the lVS1-1415 polymorphism, and the rare form of the lVS1-1505 polymorphism."

Conclusion

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

22. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

23. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
06 April 2004